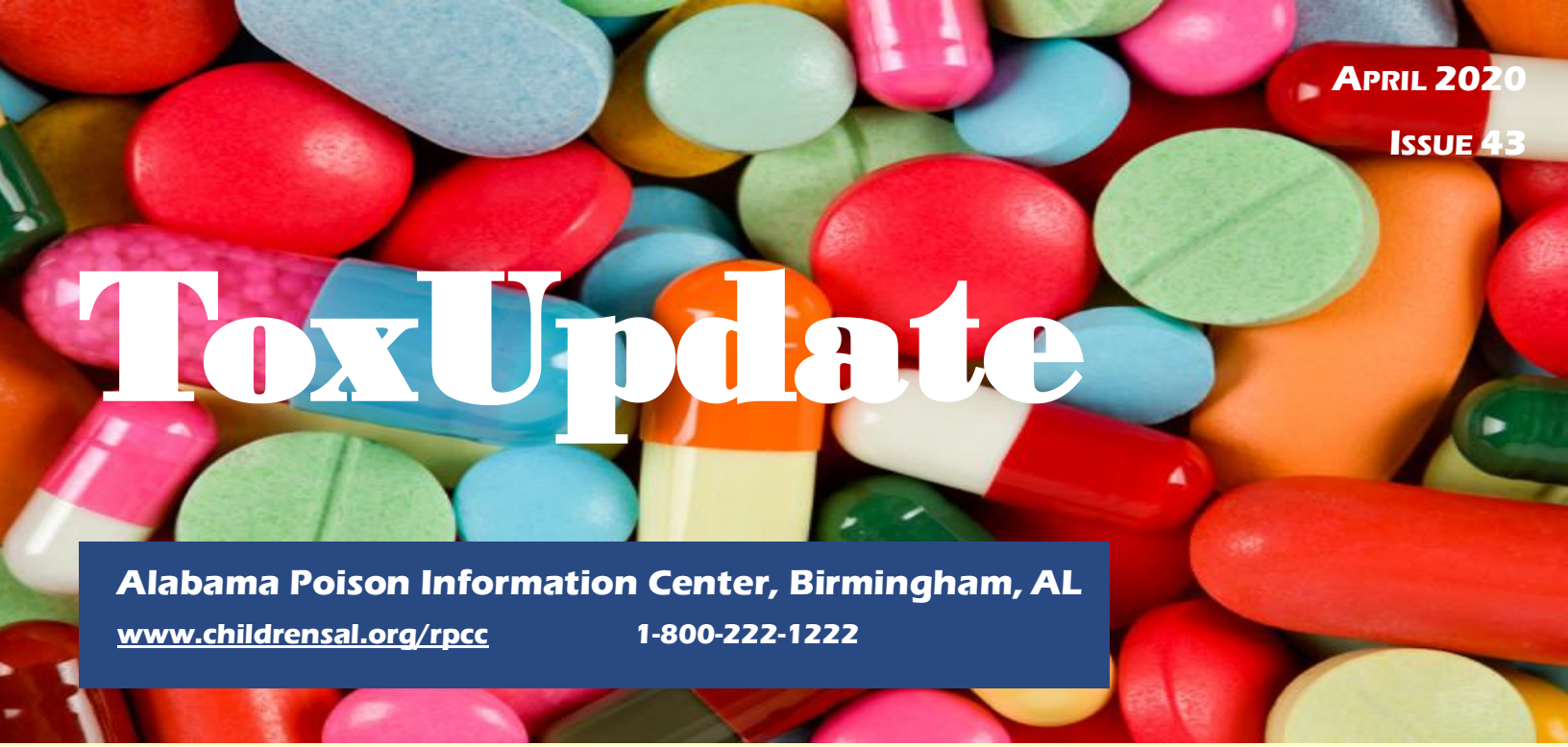

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ToxUpdate

Alabama Poison Information Center, Birmingham, AL
www.childrensal.org/rpcc 1-800-222-1222

Toxicology of Hydroxychloroquine and Chloroquine

By Laura Read, RPh, CSPI, Alabama Poison Information Center

Hydroxychloroquine (Plaquenil®) and chloroquine have a relatively narrow therapeutic index, with cardiac toxicity that includes QTc prolongation and sodium-channel inhibition, resulting in ventricular arrhythmias, conduction blockade and cardiovascular failure. Chloroquine and other medications in this medication class work by blocking the synthesis of DNA and RNA. Hydroxychloroquine, also in this class of drugs, is considered less potent but works the same way.

Chloroquine's primary use is for prophylaxis or treatment of malaria. Chloroquine and hydroxychloroquine are the only drugs that are available in the United States that are used for malaria. The drugs may also be used in the treatment of rheumatoid arthritis, lupus, and can also be used to treat liver infection caused by protozoa (extraintestinal amebiasis).

In overdose, chloroquine has quinidine-like effects. Chloroquine depresses cardiac contractility and shifts potassium from extracellular to intracellular compartments resulting in hypokalemia. In large overdoses, severe symptoms may develop in one to two hours and mortality is reported as 10% to 30%. According to the FDA, the medications are very rapidly absorbed and toxic symptoms may occur within 30 minutes in accidental overdosages and in hypersensitive patients. In a chloroquine overdose, the triad of hypotension, hypokalemia and QRS prolongation can be observed.

Chlorquine and hydroxychloroquine are contraindicated in the following: retinal or visual field changes of any etiology; porphyria and psoriasis, drug is known to precipitate severe attacks; hepatic disease; G6PD deficiency; diabetes, drug can cause severe hypoglycemia; and any known history of cardiac complications.

In the pediatric population, an overdose of chloroquine and hydroxychloroquine is most often characterized by rapid clinical deterioration. (*Continued on Page 3*)

ALABAMA POISON INFORMATION CENTER
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Special Interest Articles

Did you know?

On March 16, 2020, Regional Poison Control Center changed their name to Alabama Poison Information Center (APIC). The APIC was the 14th center established in the United States and was established in 1958. The center handles 50,000 calls a year and 60,000 follow up calls. The APIC is open 24 hours a day.

Diclofenac- Prescription to Over-the-Counter Switch

By Shalisa Whitely, Samford University PharmD Candidate

"From a toxicology standpoint, with increased access to diclofenac gel, there is heightened concern for accidental ingestions- especially in the pediatric population."

It has been reported that nonprescription medications now account for over sixty percent of all medications used in the United States and are used to treat over 400 ailments. The availability of over-the-counter (OTC) products makes it possible for the general public to treat a variety of conditions without the close supervision of a healthcare professional. Periodically, the Food and Drug Administration (FDA) will approve certain prescription medications for reclassification to over-the-counter status. This process is called "Rx to OTC" switch. An Rx to OTC switch happens when a drug manufacturer requests their product be available to purchase without a prescription. For this to happen, the manufacturer must submit documentation to the FDA proving their product(s) are safe for use by the general public and can be effectively used for self-medication. One product recently receiving this reclassification is Voltaren® Arthritis Pain.

Voltaren, generic name diclofenac, is a nonsteroidal anti-inflammatory medication (NSAID). It is available, by prescription, in many dosage forms, but the over-the-counter product will be a 1% topical gel, 100-gram tube (10 mg of diclofenac per gram). This medication is approved for the management of acute pain associated with arthritis. Diclofenac works by inhibiting the enzymes cyclooxygenase (COX)- 1 and 2. Under normal conditions, these enzymes facilitate the formation of pro-inflammatory mediators resulting in pain at the joints affected by arthritis. In the presence of diclofenac, COX-1 and 2 are inactive therefore decreasing painful inflammation. While diclofenac is not a cure for arthritis, it is effective for episodic pain in arthritic joints that respond to topical treatment. Most commonly reported adverse effects are dermatologic in nature, and include application site pain, rash, pruritus, contact dermatitis, etc.

From a toxicology standpoint, with increased access to diclofenac gel, there is heightened concern for accidental ingestions- especially in the pediatric population. According to the 2019 Regional Poison Control Center Annual Report, topical preparations are the fifth leading pediatric exposure. Currently, there is no definitive data that correlates amount of NSAID ingested to onset of clinically toxic effects. However, significant toxicity associated with NSAIDs, like diclofenac, has been reported at five to ten times the therapeutic dose. Following ingestion, patients can present with complaints of GI upset, drowsiness, and disorientation. With severe intoxication, seizure, coma and renal failure can occur as well. In fact, a 2011 article in *Open Access Emergency Medicine* described two cases in which diclofenac exposure resulted in toxicity. Both individuals involved consumed upwards of two grams of diclofenac; which is greater than the 200 mg/day maximum dose for adults. Each patient required medical attention and experienced acute renal failure during their course of treatment.

Best practice is to store all medications in a safe, secure area and out of reach of children. In the event of an NSAID exposure, whether pediatric or adult, contact your local Poison Control Center for triage and treatment recommendations.

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Nayzilam® - The First Rescue Treatment for Cluster Seizures

By Shalisa Whitely, Samford University PharmD Candidate

Acute Repetitive Seizures (ARS) or "cluster seizures" is a condition where an epileptic person experiences greater than three seizure episodes within a 24-hour period and is observed in approximately 3% of the epilepsy population. ARS tends to occur most often in very young (0-4 years) pediatric patients, approximately 5.9 per 10,000 of the general pediatric population. Given the lengthy recovery associated with seizure clusters, and the amount of neurological damage they can cause, short-term or rescue medication should be administered as soon as possible. However, there are few anti-epileptic drugs that can be administered during a seizure that are not given orally. For this reason, UCB Incorporated developed a rescue medication for this condition. On May 20, 2019, the Food and Drug Administration approved Nayzilam® (midazolam), an anti-epileptic drug, for the treatment of seizure clusters.

Unlike other anti-epileptic drugs, Nayzilam is delivered as a single dose intranasal spray. It is not necessary to prime before use. Each actuation delivers 5mg of midazolam per 0.1 ml. The most common adverse effects reported following administration include somnolence, headache, nasal discomfort, throat irritation, and rhinorrhea. While Nayzilam is the first of its kind, it is purely a rescue medication. It is not intended to replace maintenance anti-epileptic medication; which is the best way to stay ahead of seizure activity.

Overdose of midazolam can lead to respiratory and central nervous system depression. Patients may be difficult to arouse and have trouble breathing. Other signs and symptoms of midazolam overdose include slurred speech, lethargy, ataxia, and coma.

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Hydroxychloroquine and Chloroquine continued from Page 1

Symptoms may progress in one to three hours to apnea, seizures and death from cardiorespiratory arrest. Chloroquine is a potentially lethal drug even with a minimal exposure of one to two tablets (dose as low as 300 mg) in children.

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On February 26, 2020, Samford Pharmacy student, **Shalisa Whitely**, visited Adamsville Senior Citizen Center and discussed Medication Safety. Door prizes were given out and fun was had by all!